Remarks

Claims 4-6, 10-12 and 17-19 are pending. Claims 1-3, 7-9 and 13-16 have previously been canceled. Claims 4, 10, and 17 have been amended.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 4-6 and 17-19 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Legal Standard

The Court of Appeals for the Federal Circuit (CAFC) has described the legal standard for enablement under § 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art, without undue experimentation (*See, e.g.*, *Amgen v. Hoechst Marion Roussell* 314 F.3d 1313 (Fed. Cir. 2003; *Genentech, Inc. v. Novo Nordisk A/S*, 108 F3d at 165, 42 USPQ2d at 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *In re Fisher*, 427 F.2d at 839, 166 USPQ at 24; *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); *In re Stephens*, 529 F.2d 1343 (CCPA 1976)). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (*M.I.T. v. A.B. Fortia*, 774 F.2d 1104 (Fed. Cir. 1985)). In addition, as affirmed by the Court in *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524 (Fed. Cir. 1987), a patent need not teach, and preferably omits, what is well known in the art.

Whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See *In re Wands*, 858 F.2d 731, 735, 736-737, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir.1988). As set forth in *Wands*, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. In cases that involve unpredictable factors, "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

A proper analysis of the *Wands* factors shows that claims 4-6 and 17-19 satisfy the enablement requirement. Applicants do not understand how the Examiner can allege that the claims are obvious, and then suggest that they are not enabled! The quantity of experimentation necessary to obtain and use the claimed angiogenesis inhibitors for the treatment of the recited disorders is **not undue.**

The angiogenesis inhibitors that may be used in the claimed methods are disclosed in the specification on page 6, line 4 to page 7, line 10 along with a number of references which thoroughly describe these agents and **effective amounts for use in humans, and methods of administration**. In addition, the specification also teaches how to make pharmaceutical compositions of the compounds and methods that can be used to administer the drugs to patients

(see, for example, pages 12-14). Furthermore, the specification lists the diseases that may be treated on page 5, line 15 to page 6, line 2. These diseases are also well-known and characterized and can be found in any medical textbook.

The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.' *In re Atlas Powder Co., v. E.I. DuPont De Nemours & Co.* , 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir.1984). There is no requirement for examples nor is there any need for examples in this application. The claimed agents are known (although **not** for the treatment of the recited disorders), well-characterized and commercially available. Therefore, one of ordinary skill in the art could routinely arrive at an effective amount of the drugs and method of delivery to treat the claimed disorders. Furthermore, as discussed below, the term "effective amount" is a common and generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without undue experimentation, as is the case here.

In summary, it is clear from the guidance in the specification, the state of the prior art, and the level of skill in the art that one of ordinary skill in the art would be able to use the claimed angiogenesis inhibitors to treat the recited disorders without undue experimentation.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 4-6 and 10-12 and 17-19 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection.

The disorders recited in claims 4 and 10 are very well known and one of ordinary skill in the art would know what symptoms are associated with them. One can consult a number of medical textbooks and journals, as well as internet sites such as WebMd or Pubmed, to find a thorough description of the symptoms of any of these disorders. A patent need not teach, and preferably omits, what is well known in the art. *In re Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524 (Fed. Cir. 1987).

The rejection of the claims over the term "effective amount" is legally improper. "Effective amount" is a common and generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without undue experimentation. (See, e.g., *Geneva Pharmaceuticals, Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373 (Fed. Cir. 2003); *In re Halleck*, 57 C.C.P.A. 954, 422 F.2d 911, 914 (CCPA 1970). An effective amount of the angiogenesis inhibitor is an amount as required to alleviate the symptoms of the particular disorder being treated (page 14, lines 28-29). Since the claimed angiogenesis inhibitors are known and characterized compounds (although not for the treatment of the recited disorders), one of ordinary skill in the art could arrive at an "effective amount" of any one of these drugs to treat the listed disorders.

Rejection Under 35 U.S.C. § 102

Claims 10-12 and 18 were rejected under 35 U.S.C. § 102(e) as being anticipated by PCT Publication No. 95/18606 by Aggarwal ("Aggarwal") evidenced by Doland's Medical Dictionary. Claim 17 was rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,015,804 to Golub et al. ("Golub"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 10 has been amended to re-introduce previously deleted disorders and to recite that the method to treat the selected disorders comprises administering an effective amount of a pharmaceutical composition comprising a curcuminoid in combination with a pharmaceutically acceptable carrier for topical administration to inhibit angiogenesis, wherein the carrier is an ointment containing between one-half percent (0.5%) and five percent (5%) of the curcuminoid or a polymer formulation for implantation. Support for this amendment can be found on page 5, lines 19-27; page 13, line 26 to page 14, line 8; and page 14, lines 18-21.

Aggarwal does not teach or suggest treating the claimed disorders with an ointment for topical administration containing between one-half percent (0.5%) and five percent (5%) of a curcuminoid or a polymer formulation of the curcuminoid for implantation.

Claim 17 has been amended to delete "recessive dystrophic epidermolysis bullosa". This should overcome the Examiner's rejection.

Rejection Under 35 U.S.C. § 103

Claims 4 and 5 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,733,876 to O'Reilly et al. ("O'Reilly"), in view of U.S. Patent No. 6,482,810 to Brem et al. ("Brem") and further in view of Doland's Medical Dictionary, 1994 ("Doland"). Claims 4 and 5 were also rejected under 35 U.S.C. § 103(a) as being unpatentable over O'Reilly, in view of U.S. Patent No. 5,654,312 to Andrulis et al. ("Andrulis") and further in view of Doland. Claims 4-6 were further rejected under 35 U.S.C. § 103(a) as being unpatentable over O'Reilly, in view of U.S. Patent No. 5,776,898 to Teicher et al. ("Teicher") and further in view of Doland. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 4 has been amended to delete "neurofibromatosis". This amendment should overcome the Examiner's rejections.

Claim 17 was rejected under 35 U.S.C. § 103(a) as being unpatentable over O'Reilly, in view of U.S. Patent No. 4,900,815 to Tanaka et al. ("Tanaka") and Brem and further in view of Doland. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 17 has been amended to delete "hemangioma of childhood", "neurofibromatosis", and "pyogenic granulomas".

Claims 10-12 were rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,696,147 to Galardy ("Galardy") and Arbiser et al. *J Am Acad Dermatol.* 40(6 Pt 1):925-

929, 1999 ("Arbiser 1999") in view of Thaloor et al. *Cell Growth Differ.* 9(4):305-12, 1998 ("Thaloor"). In addition, claims 10-12 and 19 were rejected under 35 U.S.C. § 103(a) as being obvious over Arbiser et al. *Mol Med.* 4(3):191-195, 1998 ("Arbiser 1998") in view of Thaloor. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

None of these references teach or suggest a method to treat the claimed disorders with an ointment for topical administration containing between one-half percent (0.5%) and five percent (5%) of a curcuminoid or a polymer formulation of the curcuminoid for implantation.

Allowance of claims 4-6, 10-12, and 17-19 is respectfully solicited.

Respectfully submitted,

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